

DRUGS AND HERBAL/VITAMIN SUPPLEMENTS WHICH CAN INTERACT WITH WARFARIN

This guide is intended as a quick reference to highlight significant interactions between Warfarin and commonly prescribed and OTC medicines. It is not intended to be exhaustive or give detailed information. For further information, prescribers should refer to the SPCC, BNF or resources offering specialised information on drug interactions.

The guide also provides information on interactions between Warfarin and commonly used herbal and vitamin supplements. Where concomitant use is required, close monitoring is essential and the dose adjusted where necessary.

Drugs which increase anticoagulant effects of Warfarin

Interacting Drug	Additional Comment
Alcohol	Fluctuations in INR particularly in heavy drinkers or those with liver disease
Allopurinol	Anticoagulant effects possibly enhanced – monitor closely
Amiodarone	Slow onset – may persist long after Amiodarone is stopped. Monitor closely
Amitriptyline	Can cause unpredictable increases or decreases in INR – monitor closely
Aspirin	Avoid Aspirin as analgesic, use Paracetamol as safer alternative. Low dose Aspirin 75-100mg appears not to interact significantly
Azapropazone	Significant – avoid concomitant use
Bezafibrate	Reduce Warfarin dose by one third to a half initially and adjust accordingly – monitor closely
Cefaclor	Cefalexin, Cefradine and Cefuroxime are safer alternatives
Celecoxib	Rare cases of increased INR and bleeding – monitor closely
Ciprofibrate	Reduce Warfarin dose by one third to a half initially and adjust accordingly – monitor closely
Ciprofloxacin	Rare but unpredictable - monitor
Clarithromycin	Serious interaction but unpredictable and uncommon - use azithromycin as alternative
Clopidogrel	Increased risk of bleeding due to antiplatelet effect (Manufacturer advises avoid concomitant use)
Dexamethasone	May enhance or reduce Warfarin effects - high doses enhance
Dextropropoxyphene	Rare but unpredictable – monitor closely
Diclofenac	Increased bleeding risk with oral Diclofenac. Increased risk of haemorrhage with IV diclofenac - avoid concomitant use
Dipyridamole	Increased risk of mild bleeding due to antiplatelet effect
Erythromycin	Serious but unpredictable. Elderly at greatest risk. Monitor closely

Esomeprazole	Anticoagulant effects possibly enhanced – interactions do not appear to be clinically significant. Monitor
Fenofibrate	Reduce Warfarin dose by one third to a half initially and adjust accordingly – monitor closely
Fluoxetine	Isolated reports of raised INR and/or haemorrhage - monitor
Fluvastatin	May increase anticoagulant effects - monitor
Ibuprofen	Anticoagulant effects possibly enhanced – monitor closely
Influenza vaccine	Anticoagulant effects possibly enhanced – monitor closely
Itraconazole	Isolated reports but clinically significant – monitor closely
Ketoconazole	Monitor closely – especially in elderly
Lansoprazole	Anticoagulant effects possibly enhanced although interactions do not appear to be clinically significant. Monitor
Mefenamic acid	Anticoagulant effects possibly enhanced – monitor closely
Metronidazole	Avoid where possible. Warfarin dose may need to be reduced by up to half. Monitor closely
Miconazole	Avoid – potentially serious interaction. Use nystatin where possible
Mirtazepine	Anticoagulant effect enhanced – monitor and adjust dose
Ofloxacin	Rare but unpredictable - monitor
Omeprazole	Anticoagulant effects possibly enhanced – occasionally clinically significant interactions occur. Monitor
Orlistat	Manufacturer recommends monitoring of Warfarin dose/INR
Paracetamol	Intermittent analgesic use unlikely to affect INR (less than 2.5g/week) Prolonged regular use of high doses have been found to increase INR
Penicillin(s)*	See below*
Phenytoin	May reduce or enhance anticoagulant effects – monitor closely
Piroxicam	Monitor and reduce dose if necessary
Prednisolone	May enhance or reduce Warfarin effects -high doses enhance
Propafenone	Monitor and reduce dose if necessary
Rosuvastatin	Anticoagulant effect possibly enhanced – Monitor closely
Sibutramine	Increased risk of bleeding – monitor closely
Simvastatin	Generally small clinically irrelevant increase in anticoagulant effects. Monitor initially or after increase in Simvastatin dose
Tamoxifen	Monitor and reduce Warfarin dose as necessary (may require dose reduction of up to half)
Thyroid Hormones	Monitor and adjust Warfarin dose as necessary
Venlafaxine	Anticoagulant effects possibly enhanced – monitor closely

***Please note Penicillins and Warfarin:**

Penicillins do not normally alter the effects of Warfarin however a small number of cases of increased prothrombin times and/or bleeding have been reported in patients given Amoxicillin, Ampicillin/Flucloxacillin, Benzylpenicillin, and Co-amoxiclav.

Drugs which reduce anticoagulant effects of Warfarin

Interacting Drug	Additional Comment
Azathioprine	Monitor as Warfarin dose may need to be increased
Carbamazepine	Warfarin dose may need to be increased – monitor closely. No known interaction with oxcarbazepine
Dexamethasone	May enhance or reduce Warfarin effects -high doses enhance
Oral contraceptives	Generally avoid in thromboembolic disorders
Phenobarbitone	May require 30-60% increase in Warfarin dose. Persists for up to 6 weeks on stopping Phenobarbitone - monitor
Phenytoin	May reduce or enhance anticoagulant effects – monitor closely
Prednisolone	May enhance or reduce Warfarin effects -high doses enhance
Raloxifene	May antagonise Warfarin effect - monitor
Rifabutin	Monitor closely. Reduces anticoagulant effects within 5-7days.
Rifampicin	Warfarin dose may need to be doubled or trebled and reduced on stopping Rifabutin/Rifampicin
Vitamin K	Consider this interaction if patients are Warfarin resistant. Vit K may be present in enteral feeds, health foods, food supplements, green tea.

Reporting of drug interactions – Yellow Card

Prescribers are advised to remain vigilant for the occurrence of drug interactions with all drugs. Particular caution should be exercised when prescribing Warfarin as drug interactions are more common. If you detect an interaction with Warfarin (or any drug) we would strongly encourage you to complete a Yellow Card (back of BNF) or complete a report on the website at <http://yellowcard.mhra.gov.uk/>

Potential interactions between Warfarin and commonly used herbal and vitamin supplements.

There is increasing evidence to suggest that interactions do occur between Warfarin and herbal/vitamin supplements. Patients taking Warfarin should avoid herbal and vitamin products unless advised to do so by their doctor and only with appropriate monitoring to allow Warfarin dose adjustments where necessary.

Please note **Multivitamin supplements** should be treated with particular caution as they may contain ingredients that affect Warfarin levels. This was highlighted recently by an incident where a patient taking Seven Seas Multibionta 50+® (containing Ginseng and Bilberry) was admitted to hospital with a raised INR.

Product	Potential interaction with Warfarin
Alfalfa	Contains large amounts of Vitamin K – can reduce the anticoagulant effect of Warfarin
Bilberry	May enhance anticoagulant effect – avoid concomitant use
Chamomile	May increase the risk of bleeding
Chondroitin	Chondroitin has anticoagulant activity and should be avoided
Coenzyme Q10	Reduces anticoagulant effect as structurally similar to Vitamin K
Cranberry Juice	Possible enhancement of anticoagulant effect of Warfarin – avoid concomitant use
Devil's claw	May enhance the antiplatelet effects of Warfarin
Dong Quai	Increased risk of bleeding due to inhibition of COX and platelet aggregation. Reports of increases in INR with concurrent use
Evening Primrose Oil	May increase the risk of bruising and bleeding
Fenugreek	May increase the risk of bleeding
Feverfew	May increase bleeding especially in patients already taking certain anti-clotting medications
Flaxseed Oil	May decrease platelet aggregation and increase bleeding
Fish Oils	Fish oils have anti-platelet effects and may increase the risk of bleeding. Monitor closely
Garlic	Increased risk of bleeding due to inhibition of platelet aggregation. Do not take garlic supplements. Regular ingestion of foods containing small amounts of garlic should not pose a problem
Ginger	Large amounts may increase the risk of bleeding – until more is known, monitor INRs closely
Ginkgo Biloba	Increased risk of bleeding due to inhibition of platelet aggregation and Warfarin metabolism
Ginseng	Increased risk of bleeding due to inhibition of platelet aggregation
Glucosamine	Recent reports of increased INR in patients who had just started Glucosamine. Avoid concomitant use
Grapefruit Juice	May inhibit metabolism and increase Warfarin levels. Avoid or use cautiously

Multivitamin Supplements	Use cautiously in patients taking Warfarin – may contain ingredients that affect Warfarin metabolism eg Ginseng/Bilberry/Vit E
Red Clover	May increase the risk of bleeding
St John's Wort	Reduces anticoagulant effect of Warfarin due to increase in metabolism – avoid concomitant use
Vitamin E	Seems to inhibit platelet aggregation and antagonise the effects of clotting factors. Effects appear to be dose-dependent and are probably clinically significant with 400units/day or more

This table is intended as a quick reference to highlight common interactions between Warfarin and herbal/vitamin supplements. It is not intended to be exhaustive or give detailed information. For further information, prescribers should consult the prescribing support team or resources offering specialised information on drug interactions.

Useful websites include:

www.alternativemedicine.com

www.naturaldatabase.com

www.medicinescomplete.com